

Figure 1. N-linked Glycoprotein Structures.

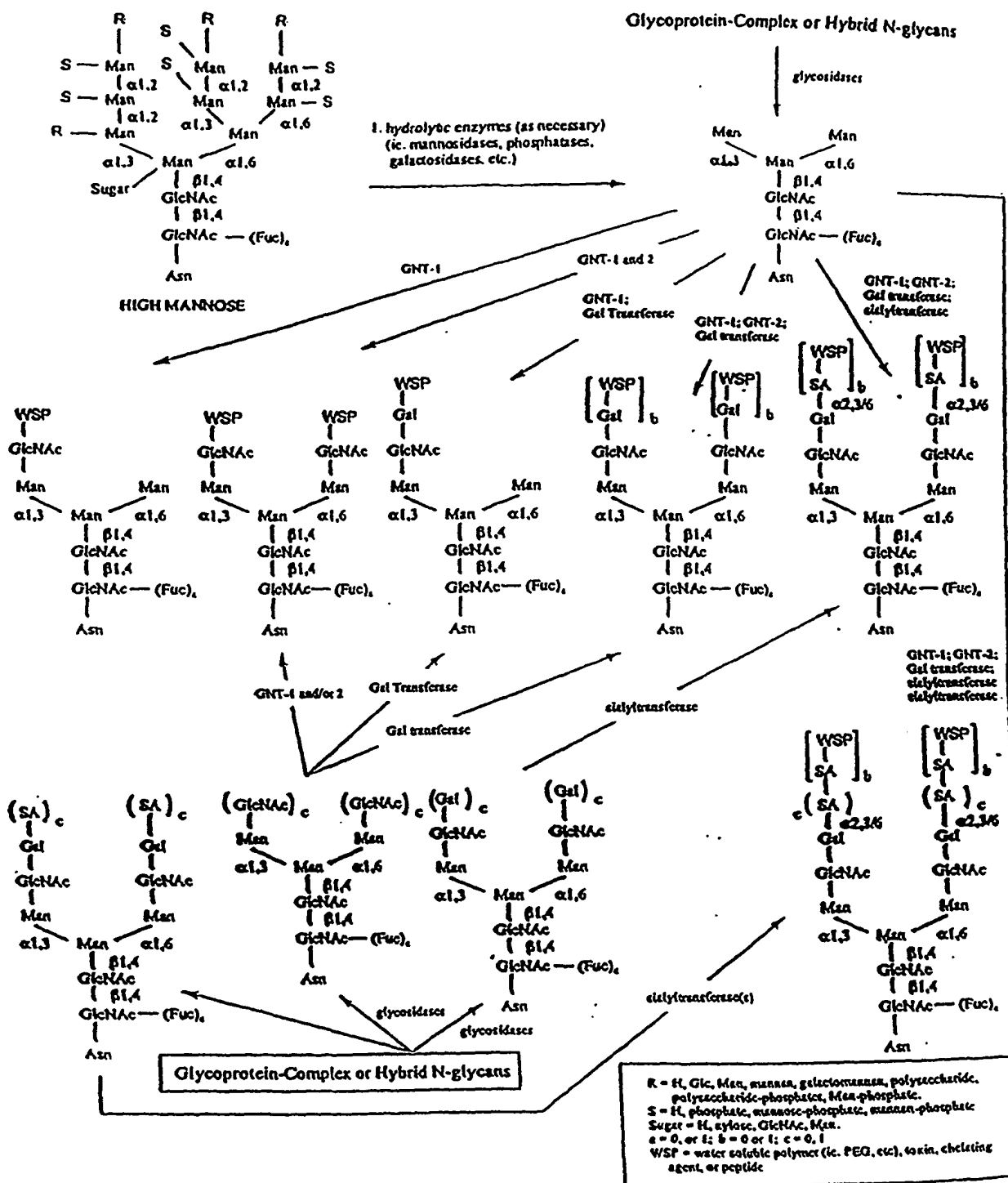


FIG. 1

Scheme 2.

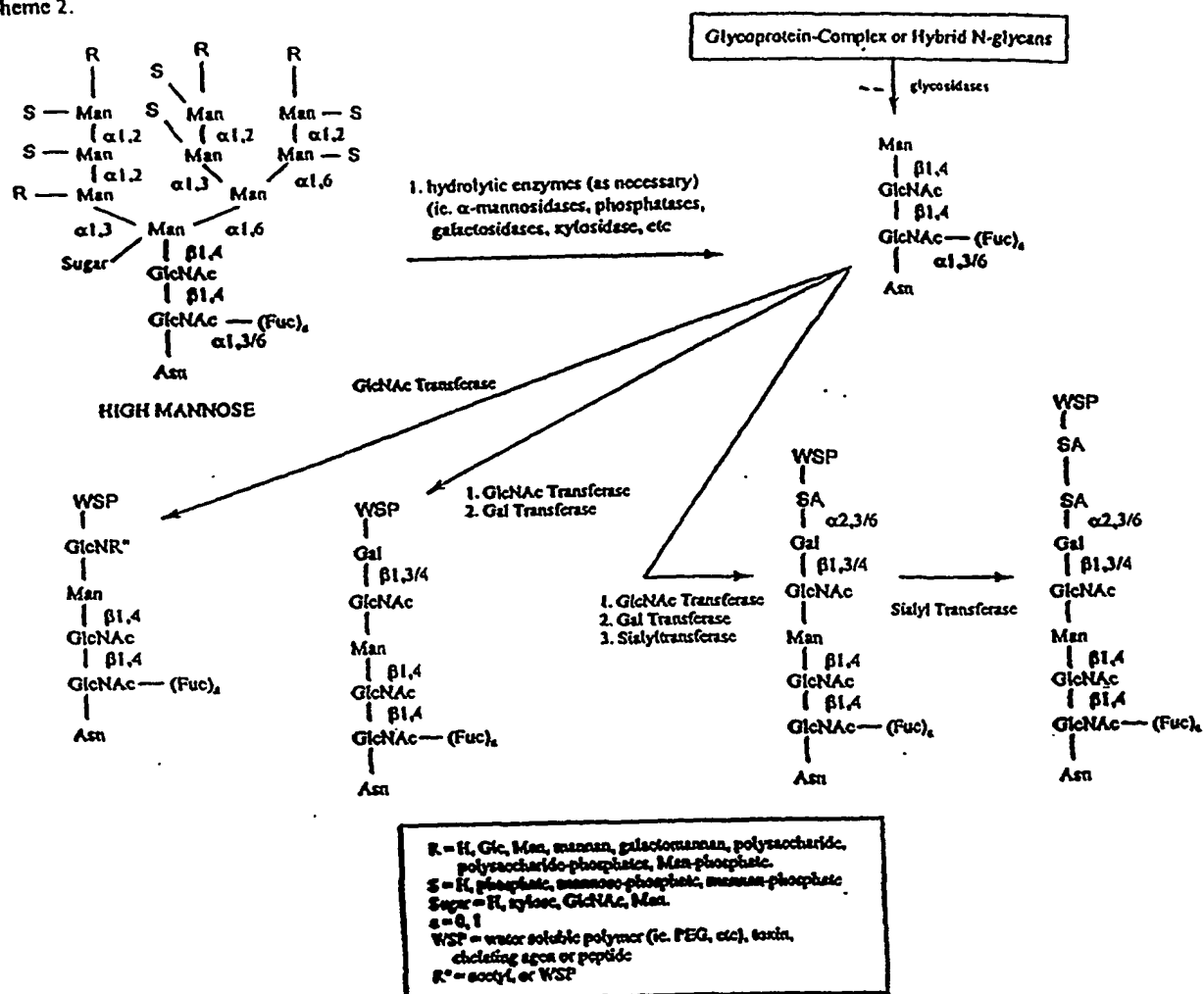


FIG. 2

Scheme 3.

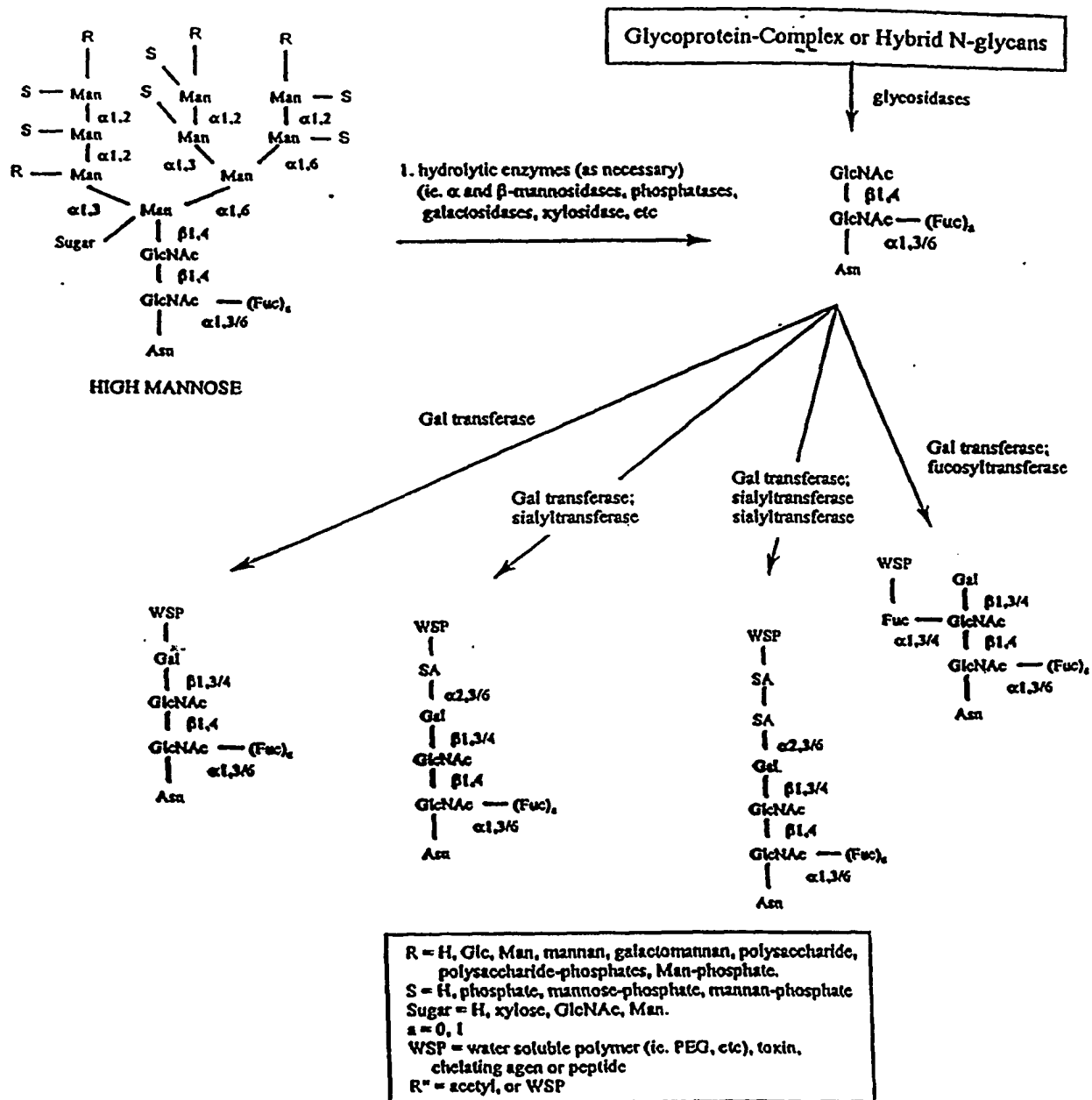


FIG. 3

Scheme 4.

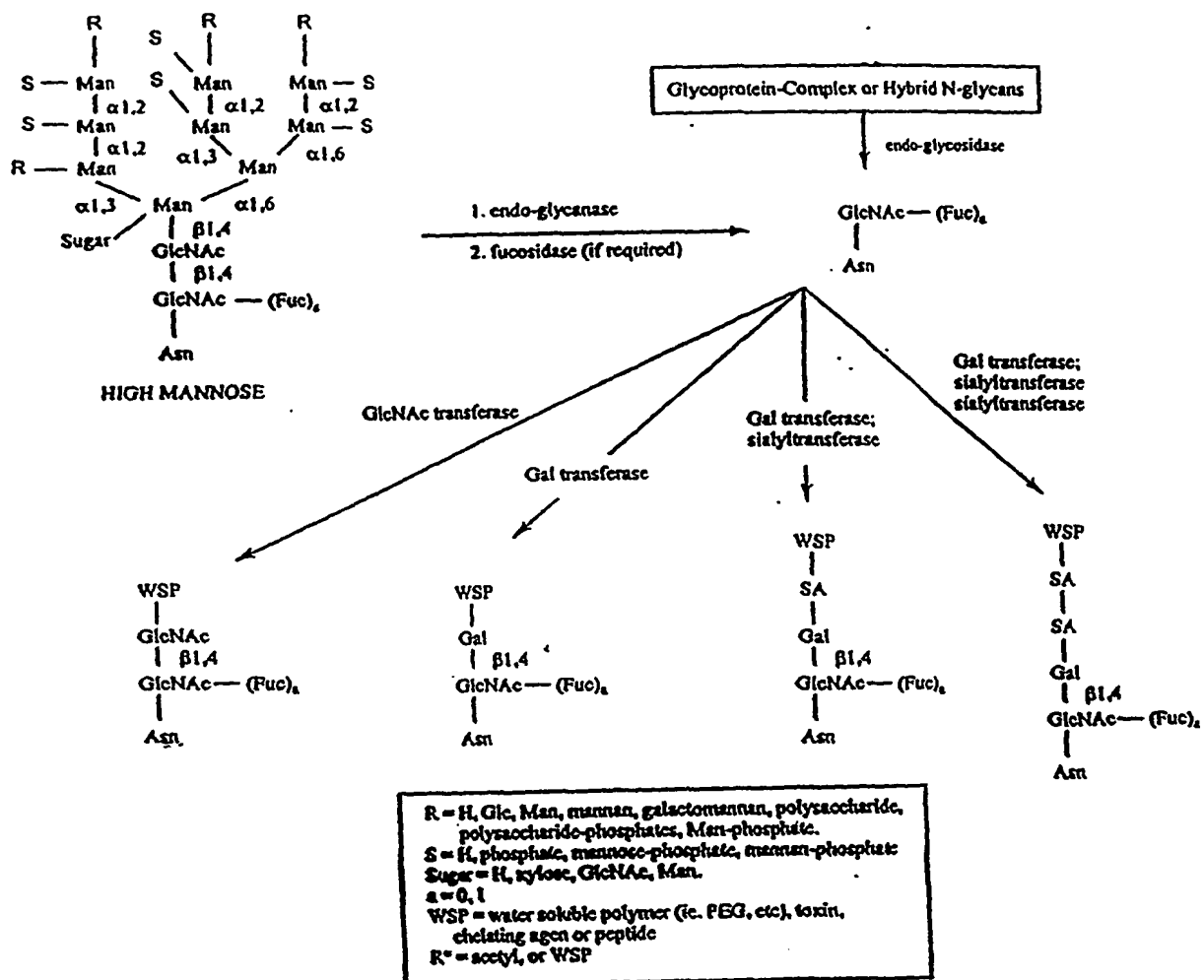


FIG. 4

Figure 5. N-linked Glycoprotein Structures.

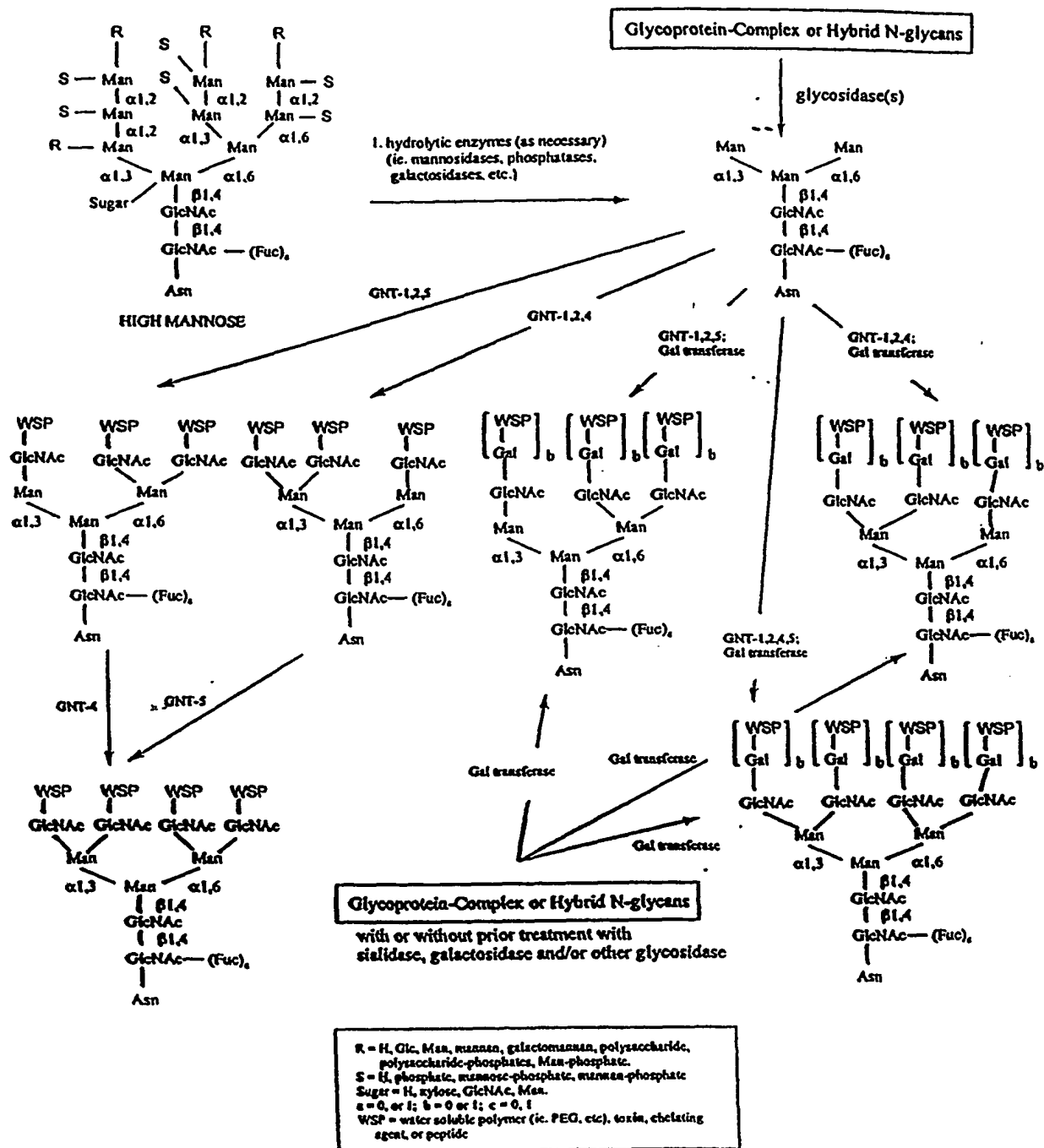


FIG. 5

Figure 6. N-linked Glycoprotein Structures.

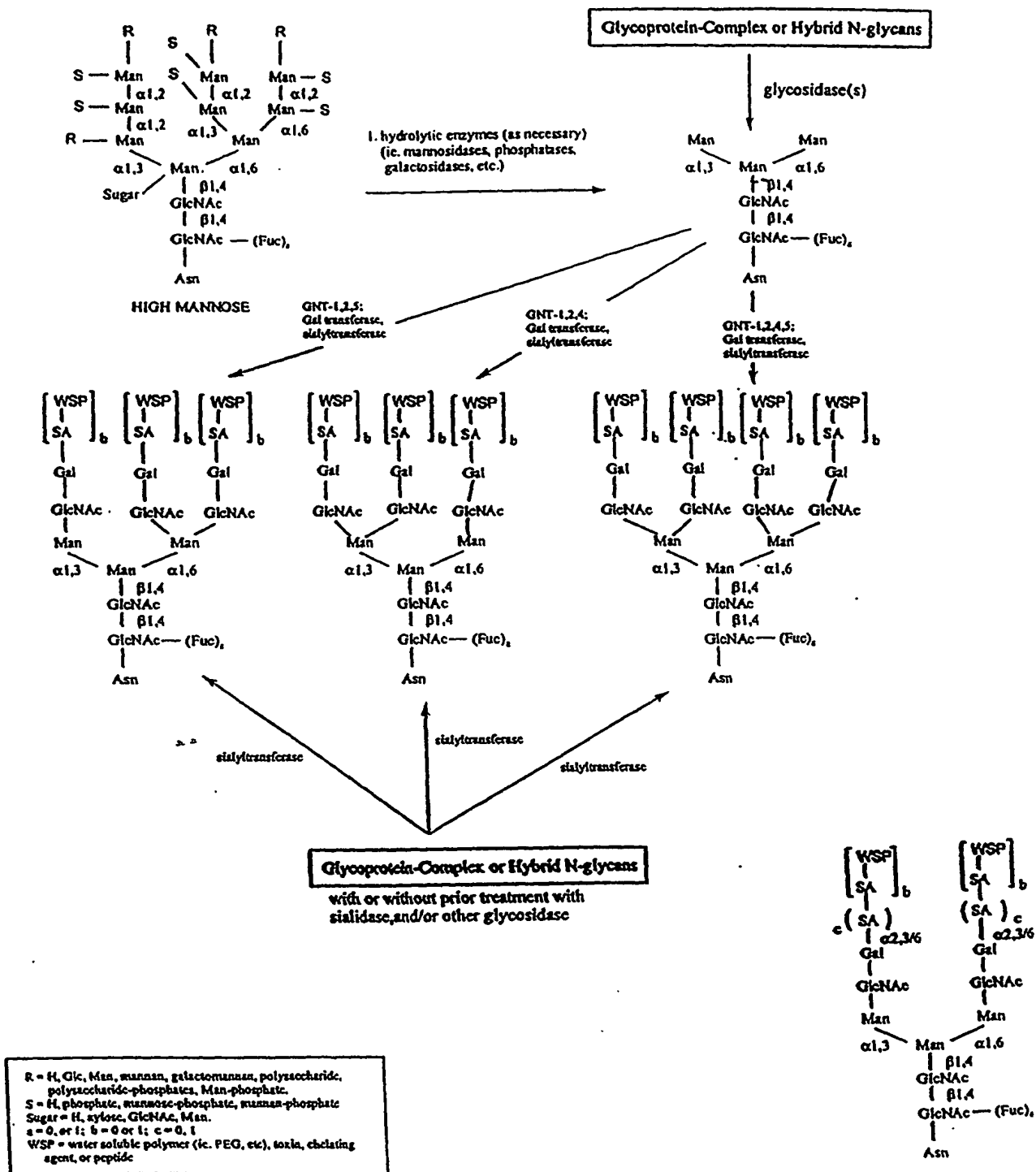


FIG. 6

Figure 7. N-linked Glycoprotein Structures.

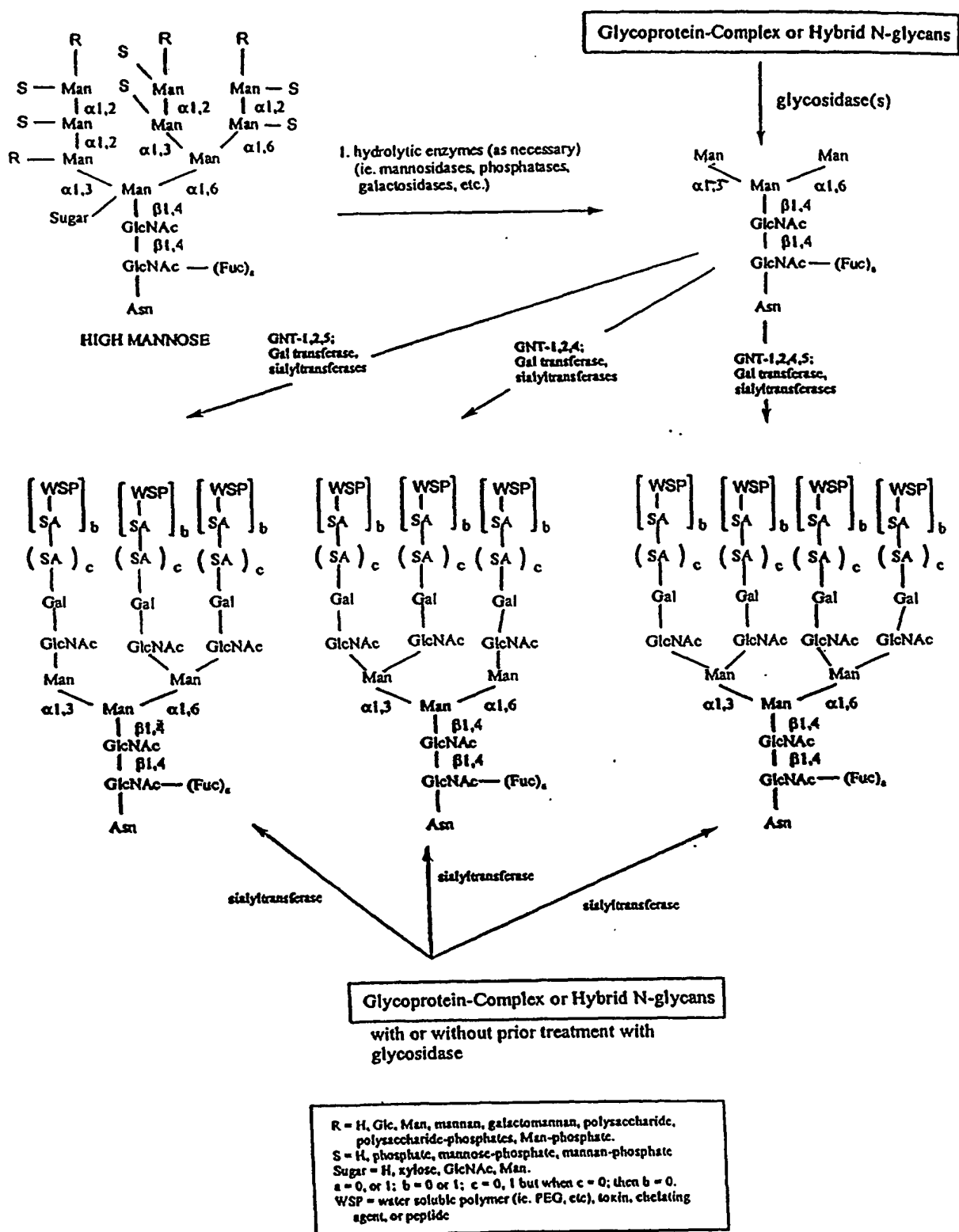


FIG. 7

Scheme 8.

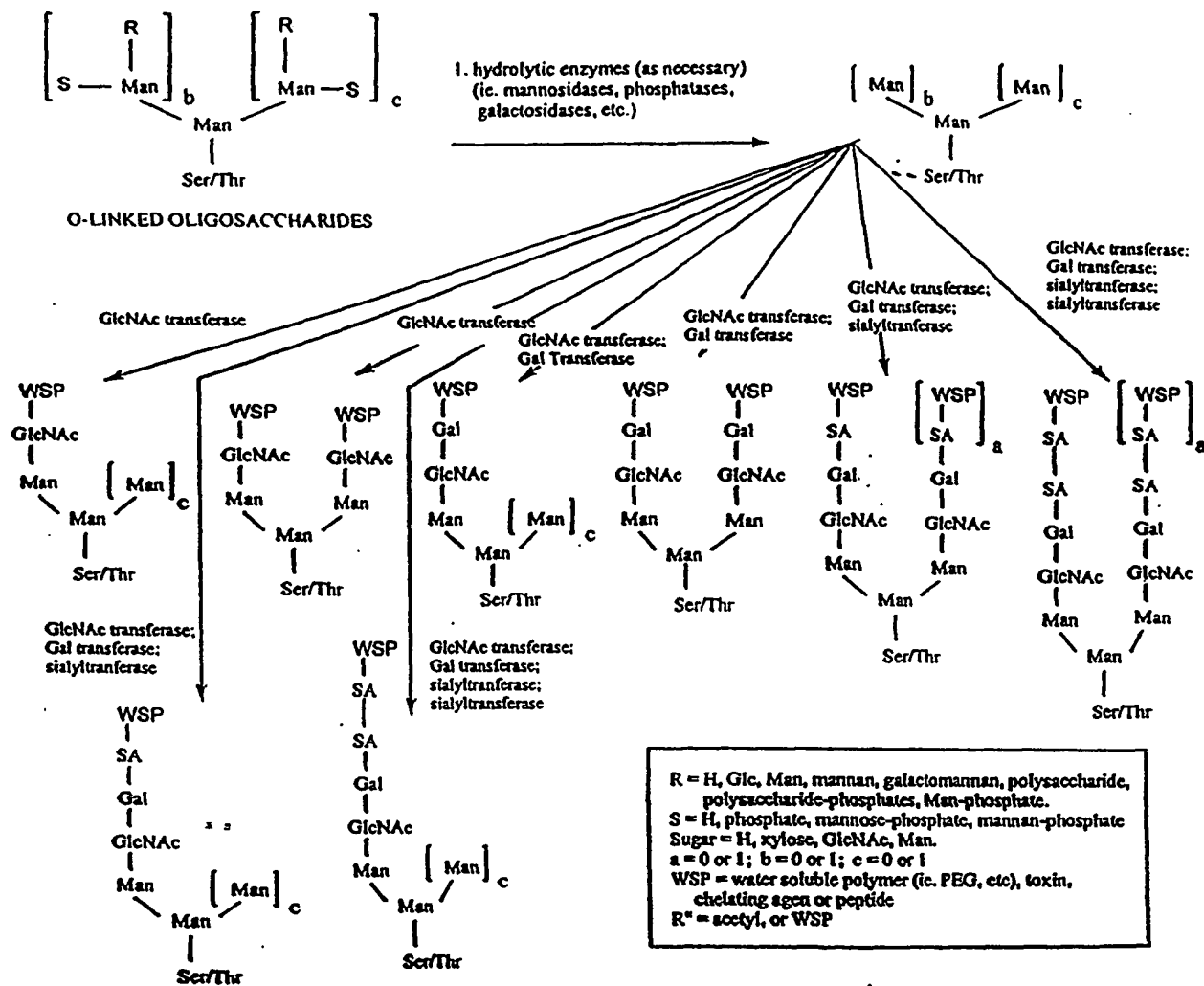


FIG. 8

Scheme 9.

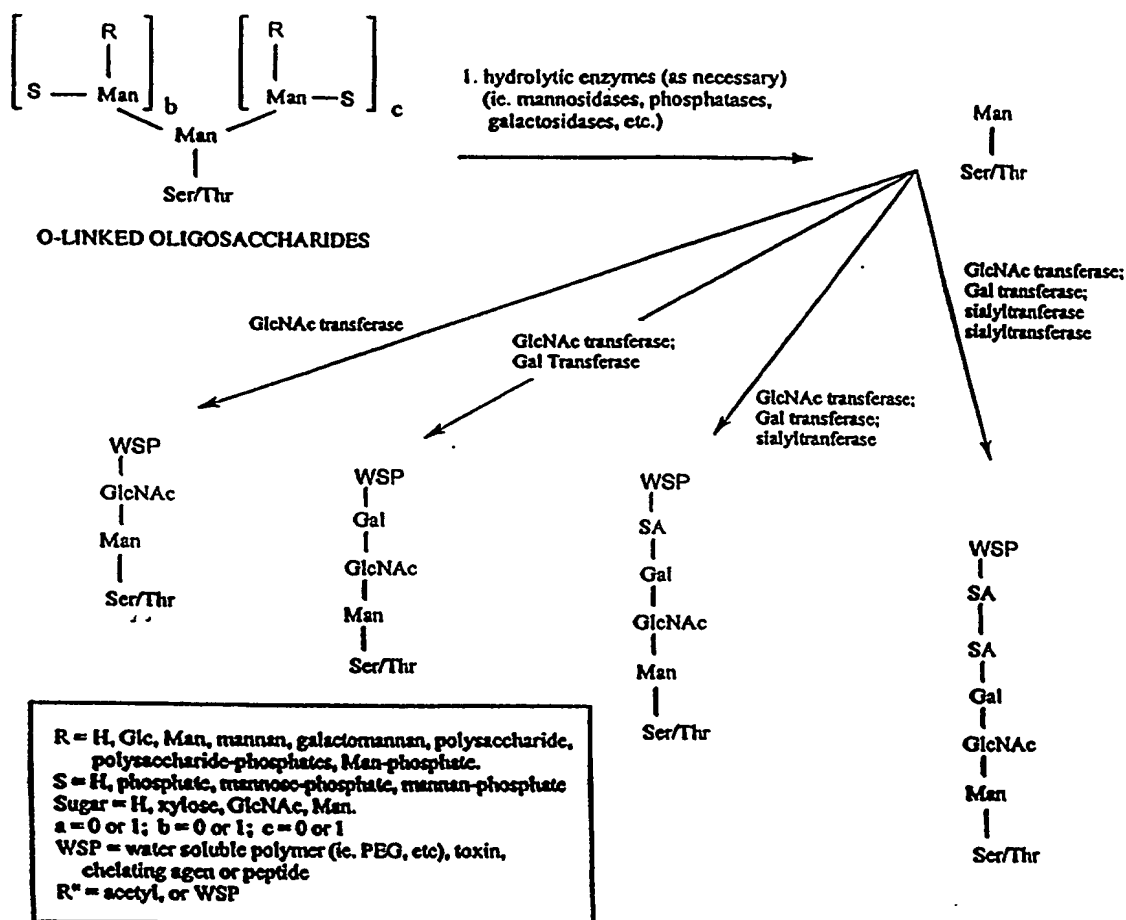
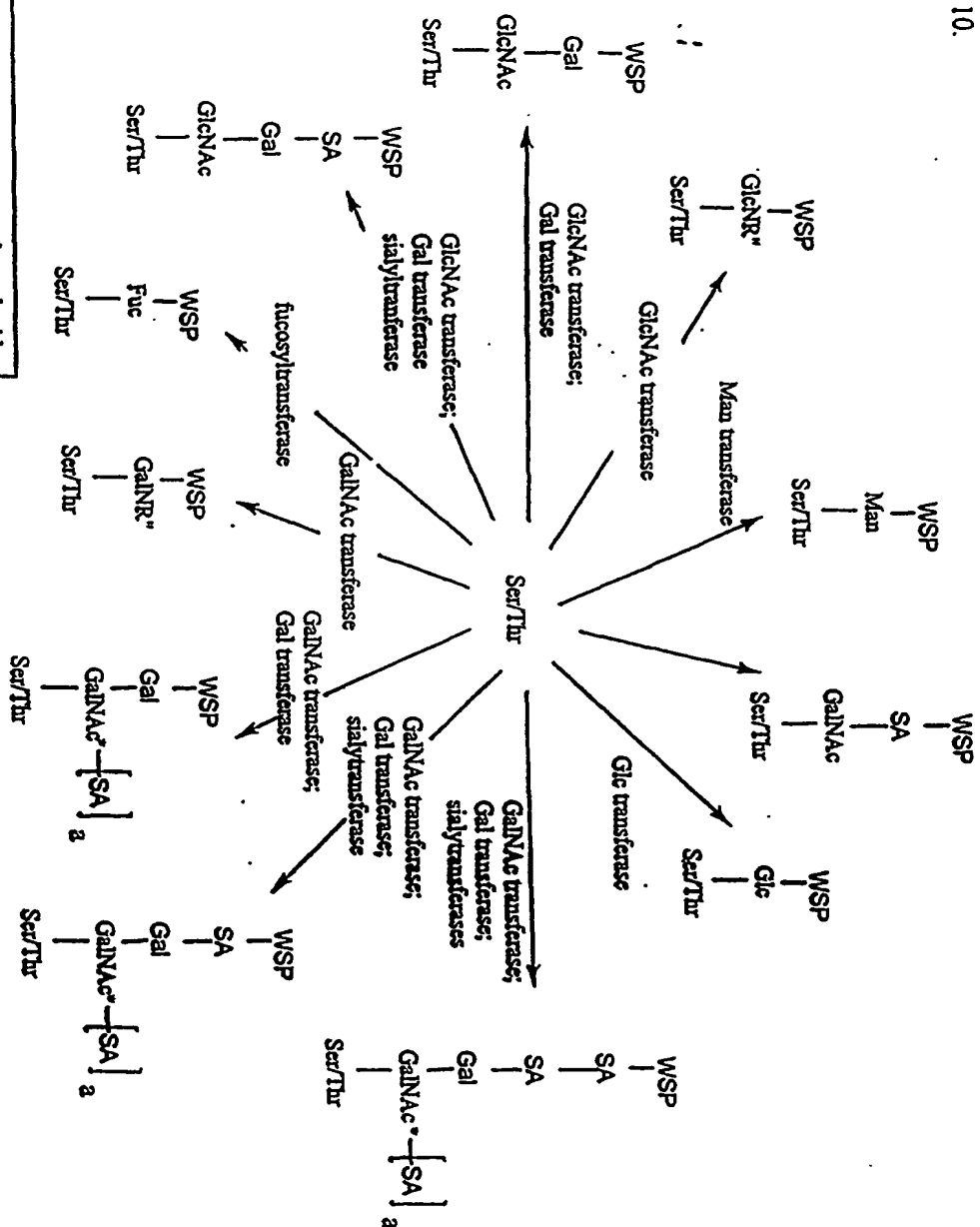


FIG. 9

Scheme 10.



R = H, Glc, Man, mannur, galactomannan, polysaccharide, polysaccharide-phosphates, Man-phosphate.
 S = H, phosphate, mannose-phosphate, mannur-phosphate
 Sugar = H, xylose, GlcNAc, Man.
 a = 0 or 1; b = 0 or 1; c = 0 or 1
 WSP = water soluble polymer (ie. PEG, etc), toxin, chelating agent or peptide
 R' = acetyl, or WSP

FIG. 10

Chemical Structure

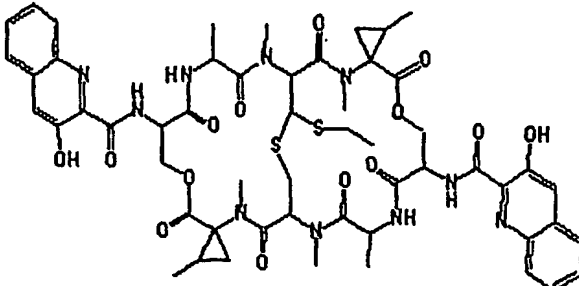
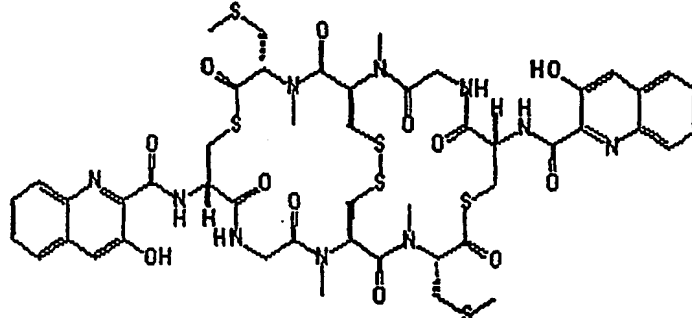
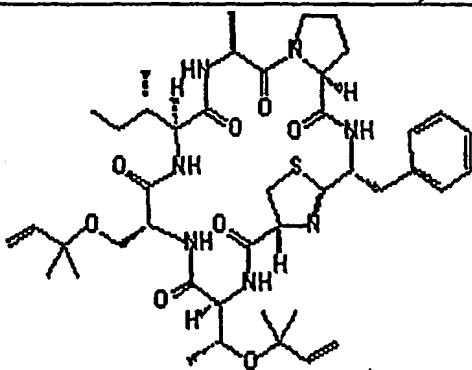
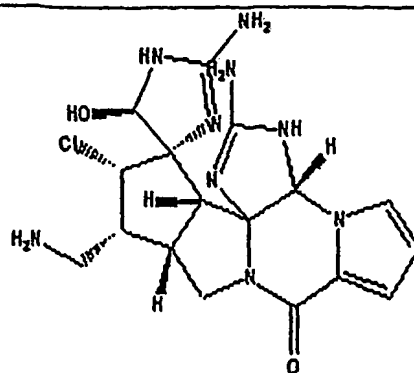
Toxin Name/ Source/ Alternate ID	CAS RN / Analog	Indication/ Toxicity	Mechanism	Activity (IC50 nM); Tumor Type
				
SW-163E/ <i>Streptomyces</i> sp SNA 15896/ SW-163E	260794-24-9; 260794-25-0/ SW-163C; SW-163A; SW-163B	Cancer and Antibacterial/ low toxicity (mice ip)	not reported	0.3 P388 0.2 A2780 0.4 KB 1.6 colon 1.3 HL-60
				
Thiocoraline/ <i>Micromonospora marina</i> (actinomycete)	173046-02-1	Breast Cancer; Melanoma; Non-small lung cancer / not reported	DNA Polymerase alpha inhibitor (blocks cell progression from G1 to S)	lung, colon, CNS melanoma
				
Trunkamide A ¹ / <i>Lissoclinum</i> sp (ascidian)	181758-83-8	Cancer/ not reported	not reported	cell culture (IC50 in micrograms/mL); 0.5 P388; 0.5 A549;

FIG. 11A

0.5 HT-29;
1.0 MEL-28

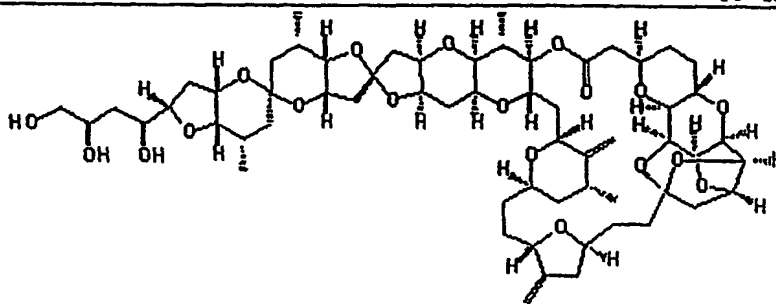


Palauamine²/
Stylorella agminata
(sponge)

148717-58-2

Lung cancer/
LD50 (i.p. in mice) is 13
mg/Kg

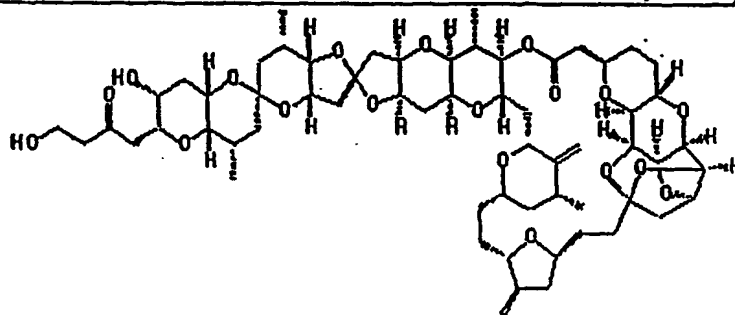
not reported cell culture (IC50 in
micrograms/mL);
0.1 P388
0.2 A549 (lung)
2 HT-29 (colon)
10 KB



Halichondrin B/
Halichondria Okadai,
Axinella Carteri and
Phanella carteri
(sponges)/
NSC-609385

103614-76-2/ cancer/
isohomohalic myelotoxicity dose
hondrin B limiting (dogs, rats)

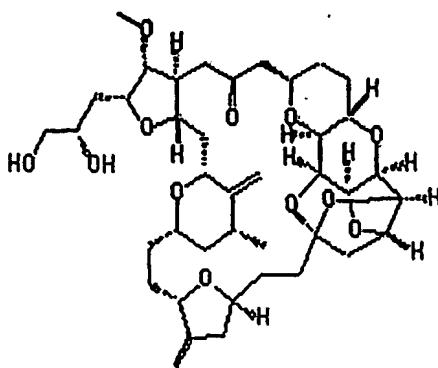
antitubulin; NCI tumor panel;
cell cycle GI(50) from 50 nM to
inhibitor 0.1 nM;
(inhibits LC50's from 40 μM to
GTP binding 0.1 nM (many 0.1 to 25
to tubulin) nM)



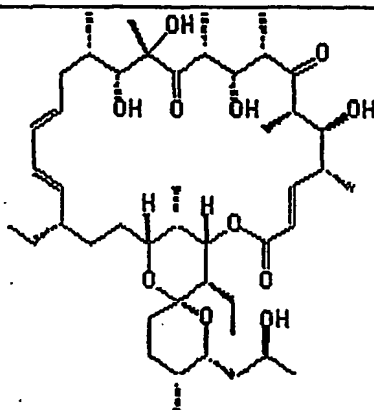
Isohomo-halichondrin B/ 157078-48-3/ melanoma, lung, CNS,
Halichondria Okadai, halichondrin colon, ovary/
Axinella Carteri and B not reported
Phanella carteri
(sponges)/
NSC-650467

antitubulin; IC50's in 0.1 nM range
cell cycle (NCI tumor panel)
inhibitor
(inhibits
GTP binding
to tubulin)

FIG. 11B



Halichondrin B analogs/ semi-synthetic starting from <i>Halichondria</i> <i>Okadai</i> , <i>Axinell Carteri</i> and <i>Phanikell carteri</i> (sponges)/ ER-076349; ER-086526; B-1793; E-7389	253128-15-3/ ER-076349; ER-086526; B-1793; E-7389	solid tumors/ not reported	tubulin binding agent; disruption of mitotic spindles	cell culture (not reported); animal models active (tumor regression observed) in lymphoma, colon (multi-drug resistant).
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NK-130119/ <i>Streptomyces</i> <i>bottropensis/</i> NK-130119	132707-68-7	antifungal and anticancer/ not reported	not reported	25 ng/mL colon 8.5 ng/mL lung
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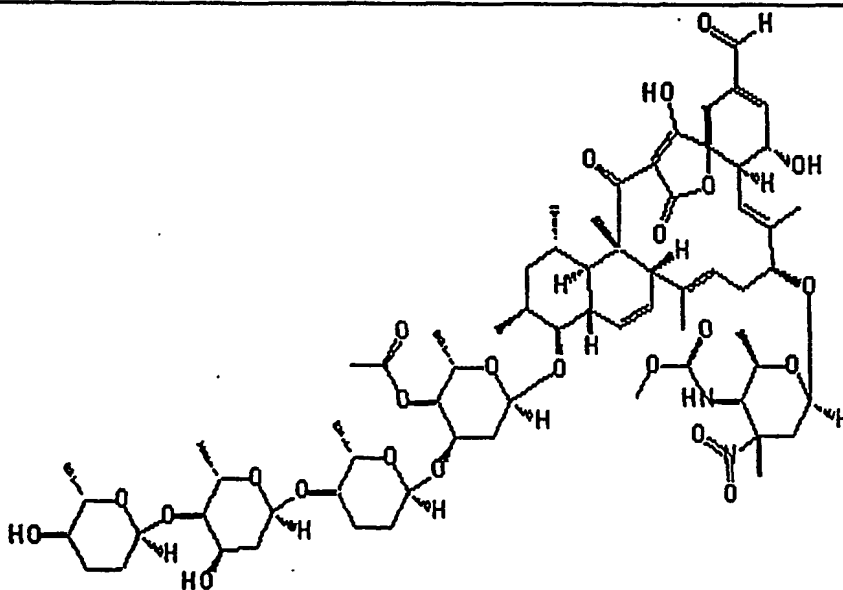


FIG. 11C

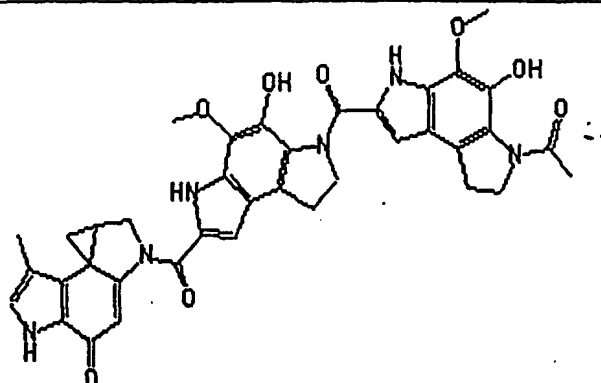
Tetrocarcin A/
not reported/
KF-67544

73666-84-9/
analogs are
reported

cancer/
not reported

inhibits the
anti-
apoptotic
function of
Bcl2

not reported



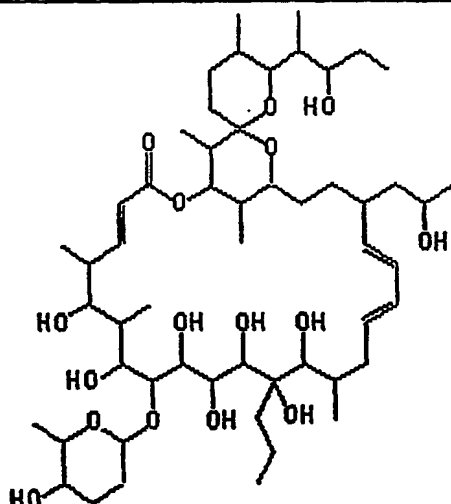
Gilvusmycin/
Streptomyces QM16

195052-09-6

cancer/
not reported

not reported

IC50's in ng/mL:
0.08 P388
0.86 K562 (CML)
0.72 A431 (EC)
0.75 MKN28 (GI);
(for all < 1 nM)



IB-96212/
marine actinomycete/
IB-96212

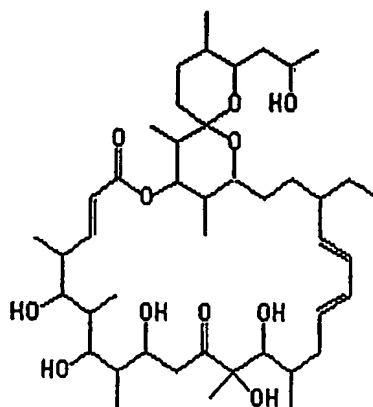
220858-11-7/
IB-96212;
IB-98214;
IB-97227

Cancer and
Antibacterial/
not reported

not reported

IC50's in ng/mL:
0.1 P388

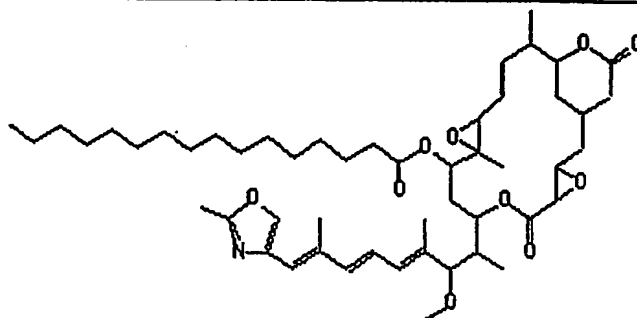
FIG. 11D



BE-56384³/
Streptomyces Sp./
 BE-56384

207570-04-5 cancer/
 not reported

not reported IC50's in ng/mL:
 0.1 P388
 0.29 colon 26
 34 DLD-1
 0.12 PC-13
 0.12 MKM-45



Palmitoylrhizoxin/
 semi-synthetic; *Rhizopus*
chinensis

135819-69-1/ cancer/
 Analog of binds LDL; less
 rhizoxin cytotoxic than rhizoxin

tubulin
 binding
 agent (cell
 cycle
 inhibitor)

not reported

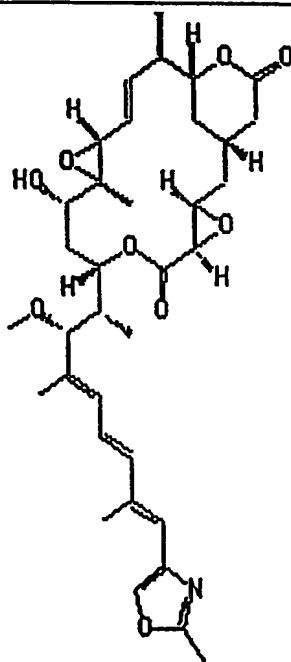
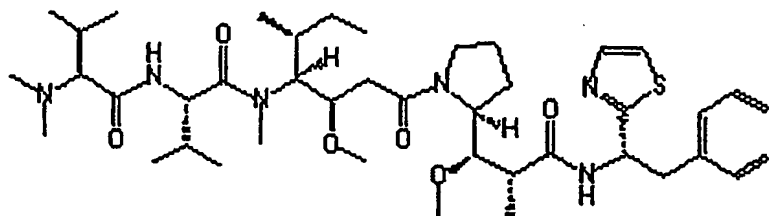
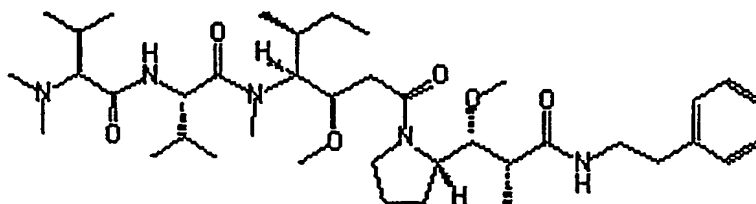


FIG. 11E

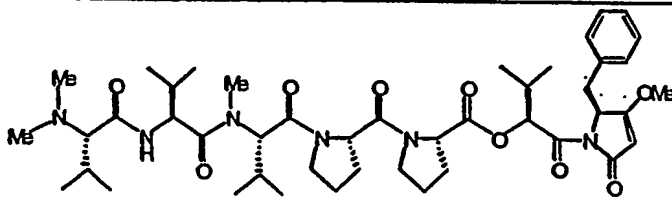
Rhizoxin/ <i>Rhizopus chinensis/</i> WF-1360; NSC-332598; FR-900216	95917-95-6; 90996-54-6	melanoma, lung, CNS, colon, ovary, renal, breast, head and neck/ Rapid Drug clearance; High AUC correlates with high toxicity	tubulin binding agent (cell cycle inhibitor)	NCI tumor panel (NSC 332598); log GI50's: 50 nM to 50 μ M; log LC50's: 50 μ M to 0.5 nM (several cell lines at 50 μ M).
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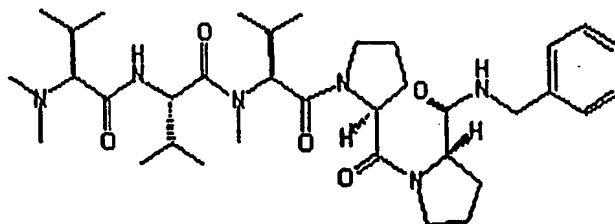
Dolastatin-10/ <i>Dolabella auricularia</i> (sea hare)/ NSC-376128	110417-88-4/ other Dolistatins (ie. 15) and analogues	prostate, melanoma, leukemia/ myelotoxicity (at greater than 0.3 pM)	tubulin binding (tubulin aggregation)	NCI tumor panel (60 cell line; GI50); 25 nM to 1 pM (most < 1 nM) (three cell lines μ M)
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soblidotin/ synthetic/ TZT-1027; auristatin PE	149606-27-9/ analogues prepared	cancer (pancreas, esophageal colon, breast, lung, etc) / MTD was 1.8 mg/Kg (IV); toxicity not reported	tubulin binding agent	cell culture: colon, melanoma, M5076 tumors, P388 with 75- 85% inhibition (dose not reported)
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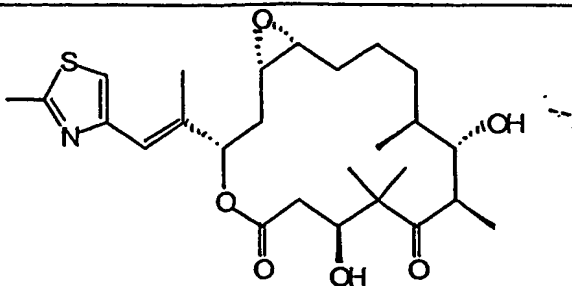
Dolastatin-15/ <i>Dolabella auricularia</i> (sea hare)	not reported/ other Dolistatins (ie. 15) and analogues	cancer/ not reported	Tubulin binding (tubuline aggregation)	NCI tumor panel (60 cell line; GI50); 25 nM to 39 pM (most < 1 nM) (one cell line 2.5 μ M); most active in breast
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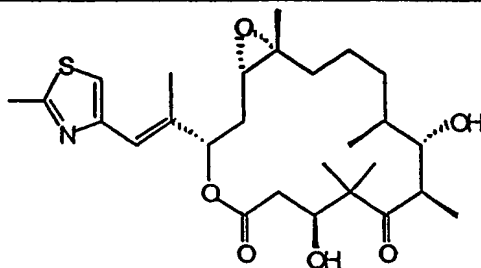
Cemadotin⁴/	1159776-69-	melanoma/	tubulin	NCI tumor panel (NCS
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FIG. 11F

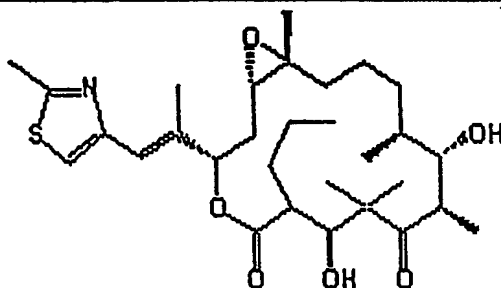
<p>Synthetic; Parent Dolastatin-15 was isolated from <i>Dolabella auricularia</i> (sea hare)/ LU-103793; NSC D-669356</p>	<p>9/ many analogs</p>	<p>hypertension, myocardial ischemia and myelosuppression were dose-limiting toxicities.</p>	<p>binding (tubulin aggregation)</p>	<p>D-669356); active in breast, ovary, endometrial, sarcomas and drug resistant cell lines. Data not public.</p>
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<p>Epothilone A/ Synthetic or isolated from <i>Sorangium cellulosum</i> (myxococcales) strain So ce90)</p>	<p>not reported/ many analogs</p>	<p>cancer/ not reported</p>	<p>tubulin binding (tubulin polymerization)</p>	<p>IC50's of; 1.5 nM MCF-7 (breast) 27.1 nM MCF-7/ADR 2.1 nM KB-31 (melanoma) 3.2 nM HCT-116</p>
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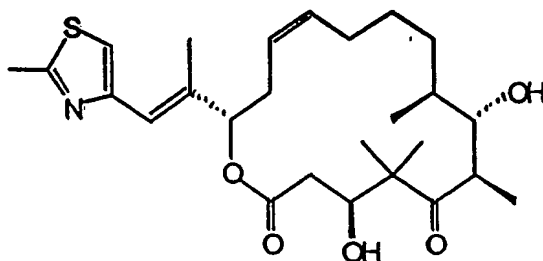


<p>Epothilone B/ Synthetic or isolated from <i>Sorangium cellulosum</i> (myxococcales) strain So ce90) / EPO-906</p>	<p>152044054-7/ many analogs</p>	<p>Solid tumors (breast, ovarian, etc)/ well tolerated; t1/2 of 2.5 hrs; partial responses (phase I); diarrhea major side effect.</p>	<p>tubulin binding (tubulin polymerization)</p>	<p>IC50's of; 0.18 nM MCF-7 (breast) 2.92 nM MCF-7/ADR 0.19 nM KB-31 (melanoma) 0.42 nM HCT-116; broad activity reported</p>
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<p>Epothilone Analog / Synthetic or semi-synthetic; Original lead, Epothilone A, isolated from <i>Sorangium cellulosum</i> (myxococcales) strain So ce90)/ ZK-EPO</p>	<p>not reported / hundreds of analogs</p>	<p>cancer/ not reported</p>	<p>tubulin binding (tubulin polymerization)</p>	<p>IC50's of 0.30 to 1.80 nM in various tumor cell lines; active in drug resistant cell lines</p>
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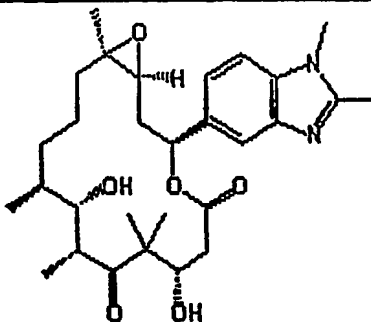
FIG. 11G



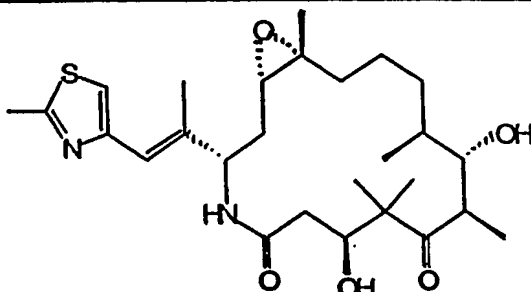
Epothilone D / Epothilone D, isolated from <i>Sorangium</i> <i>cellulosum</i> (myxococcales) strain So ce90/ KOS-862	189452-10-9/ many analogs	Solid tumors (breast, ovarian, etc)/ emesis and anemia; t1/2 of 5-10 hrs.	tubulin binding (tubulin polymeriza- tion)	NCI tumor panel (NSC- 703147; IC50); 0.19 nM KB-31 (melanoma) 0.42 nM HCT-116; broad activity reported
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Structure Not Identified

Epothilone D analog ^{5/} Synthetic or semi- synthetic; Original lead, Epothilone D, isolated from <i>Sorangium</i> <i>cellulosum</i> (myxococcales) strain So ce90/ KOS-166-24	189453-10-9/ hundreds of analogues	Solid tumors; not reported	tubulin binding (tubulin polymeriza- tion)	not reported
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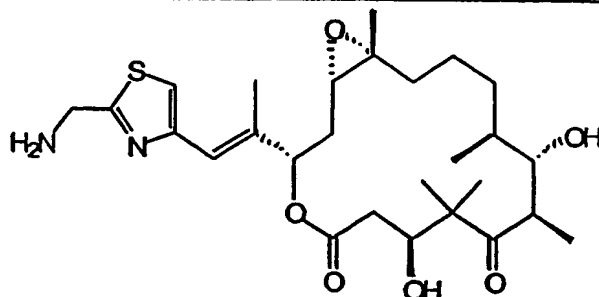
Epothilone Analog / Synthetic; Original lead, Epothilone A, isolated from <i>Sorangium</i> <i>cellulosum</i> (myxococcales) strain So ce90/ CGP-85715	not reported/ hundreds of analogues	cancer; not reported	tubulin binding (tubulin polymeriza- tion)	not reported
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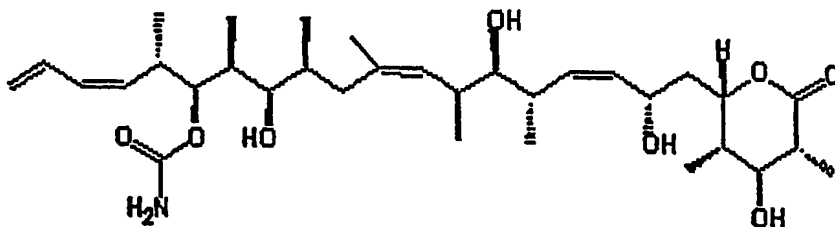
Epothilone Analog/	219989-84-1/	non-small cell Lung,	tubulin	NCI tumor Panel (NSC-
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FIG. 11H

Synthetic or semi-synthetic; Original lead, Epothilone B, isolated from <i>Sorangium cellulosum</i> (myxococcales) strain So ce90)/ BMS-247550	hundreds of analogs	breast, stomach tumor (objective responses in breast ovarian and lung)/ sever toxicity (fatigue, anorexia, nauseas, vomiting, neuropathy myalgia)	binding (tubulin polymerization)	710428 & NSC-710468); 8-32 nM (NCI data not available)
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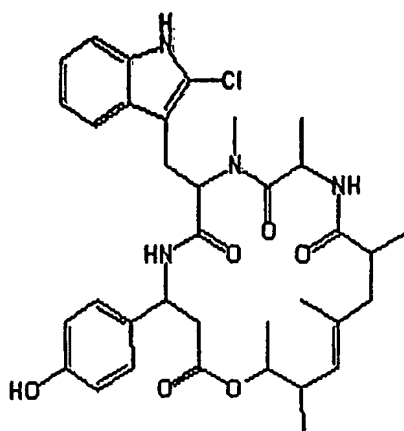


Epothilone Analog / Synthetic or semi-synthetic; Original lead, Epothilone B, isolated from <i>Sorangium cellulosum</i> (myxococcales) strain So ce90)/ BMS-310705	not reported/ hundreds of analogs	advanced cancers/ adverse events (diarrhea, nausea, vomiting, fatigue, neutropenia); t1/2 of 3.5 hrs; improved water solubility to BMS 247550.	tubulin binding (tubulin polymerization)	broad activity with IC50's of 0.7 to 10 nM
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Discodermolide / synthetic; originally isolated from <i>Discodermia dissoluta</i> (deep water sponge); rare compound (7 mg per 0.5 Kg sponge/ XAA-296	127943-53-7/ analogs less potent	solid tumors/ not reported; 100-fold increase in water solubility over taxol	tubulin stabilizing agent (similar to taxol)	Broad activity (A549-nsclung, prostate, P388, ovarian with IC50's about 10 nM) including multi-drug resistant cell lines;
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FIG. 11I



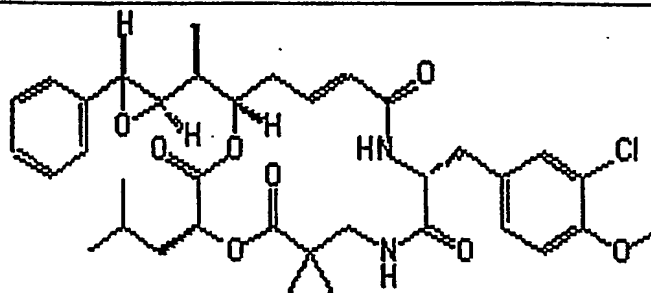
**Chondramide D/
not reported**

172430-63-6

cancer/
not reported

tubulin
binding
agent; actin
polymeriza-
tion inhibitor

5 nM A-549
(epidermoid carcinoma)
15 nM A-498 (kidney)
14 nM A549 (lung)
5 nM SK-OV-3 (ovary)
3 nM U-937
(lymphoma)



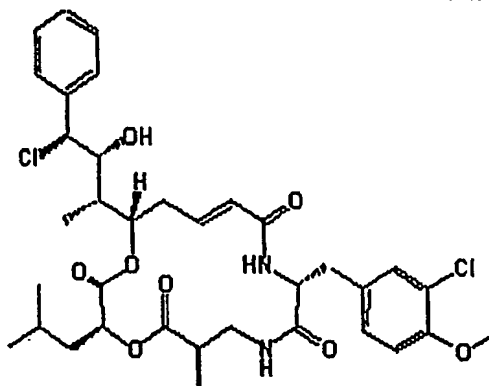
Cryptophycin analogs
(including 52, 55 and
others)^{6/}
Nostoc sp GSV 224 (blue-
green algae) isolated
Cryptophycin 1/
LY-355703; Ly-355702;
NSC-667642

204990-60-3
and 186256-
67-7/
many potent
analogs
prepared at
Lilly

solid tumors, colon
cancer/
Phase II studies halted
because of severe
toxicity with one death
resulting from drug;

tubulin
polymeriza-
tion inhibitor

broad activity (lung,
breast, colon, leukemia)
with IC50's of 2 to 40
pM; active against
multi-drug resistance
cell lines (resistant to
MDR pump). NCI
tumor panel, GI50's
from 100 nM to 10 pM;
LC50's from 100 nM to
25 pM.



Cryptophycin 8/

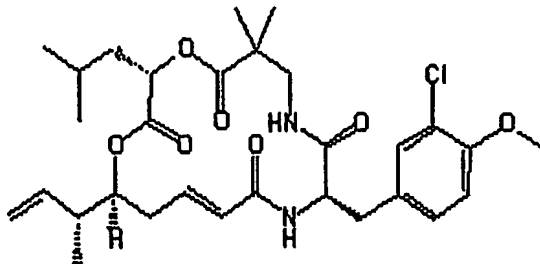
168482-36-8; solid tumors/

tubulin

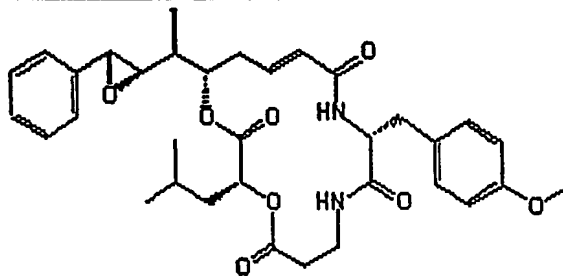
broad spectrum

FIG. 11J

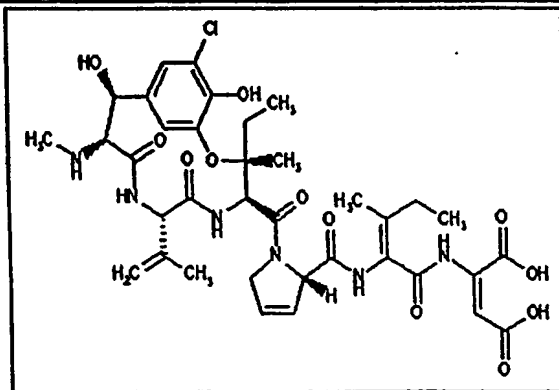
semi-synthetic; starting material from <i>Nostoc</i> sp.	168482-40-4; not reported 18665-94-1; 124689-65-2; 125546-14-7/ cryptophycin 5, 15 and 35	polymeriza- tion inhibitor	anticancer activity (cell culture) including multi-drug resistant tumors
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Cryptophycin analogs ⁷ / synthetic; semi-synthetic, starting material from <i>Nostoc</i> sp./ LY-404291	219660-54-5/ LY-404292	solid tumors/ not reported	topoisomer- ase inhibitors	not reported
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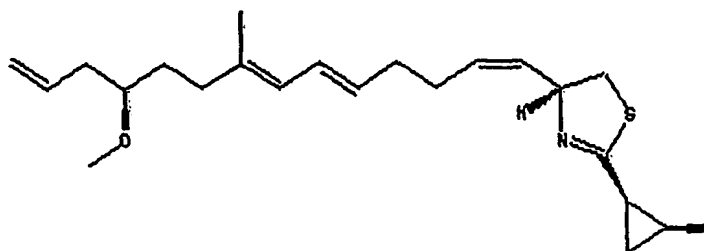


Arenastatin A analogs ⁸ / <i>Dysidea arenaria</i> (marine sponge)/ Cryptophycin B; NSC-670038	not reported/ analog prepared	cancer/ not reported	inhibits tubulin polymeriza- tion	8.7 nM (5 pg/mL) KB (nasopharyngeal); NCI tumor panel (GI50's); 100 pM to 3 pM
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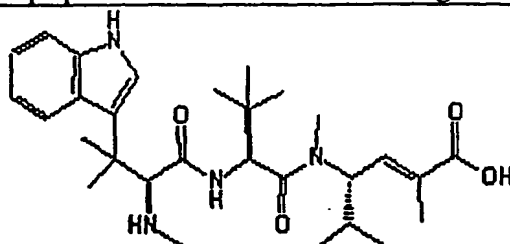


Phomopsin A/ <i>Diaporthe toxicus</i> or <i>Phomopsis leptostromiformis</i> (fungi)	not reported	Liver cancer (not as potent in other cancers)/ not reported	tubulin binding agent	potent anticancer activity especially against liver cancer
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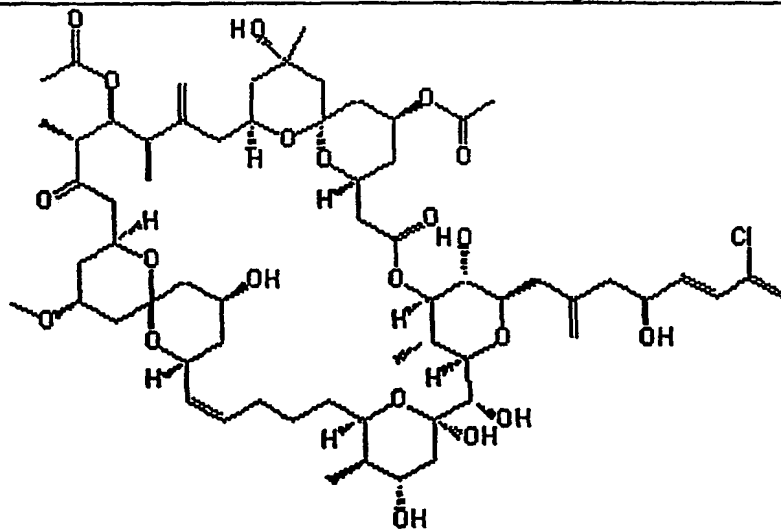
FIG. 11K



Curacin A and analogs/ <i>Lyngbya majuscula</i> (blue green cyanobacterium)	155233-30-0/ analogs have been prepared	Cancer/ not reported	Tubulin binding agent	↗ broad activity (cancer cell lines); 1-29 nM
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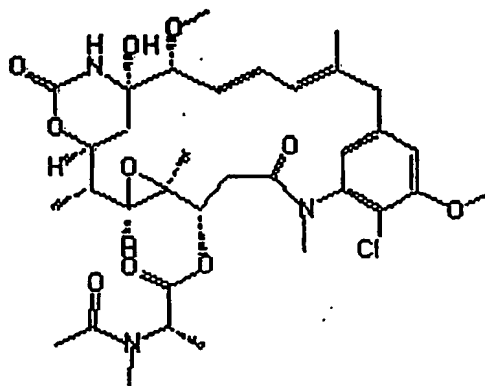


Hemiasterlins A & B and analogs ^{9/} <i>Cymbastela</i> sp.	not reported/ criamide A & B; geodiamiolid- G	Cancer/ not reported	Antimitotic agent (tubulin binding agent)	broad activity: 0.3-3 nM MCF7 (breast); 0.4 ng/mL P388
--	---	-------------------------	---	---



Spongistatins (1-9)^{10/} <i>Spirastrell spinispirulifera</i> (sea sponge)	149715-96-8; 158734-18-0; 158681-42-6; 158080-65-0; 150642-07-2; 153698-80-7; 153745-94-9; 150624-44-5; 158734-19-1/ other spongistatins	cancer/ not reported	tubulin binding agent	Most potent compounds ever tested in NCI panel cell line (mean GI50's of 0.1 nM; Spongistatin-1 GI50's of 0.025-0.035 nM with extremely potent activity against a subset of highly chemoresistant tumor types
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FIG. 11L



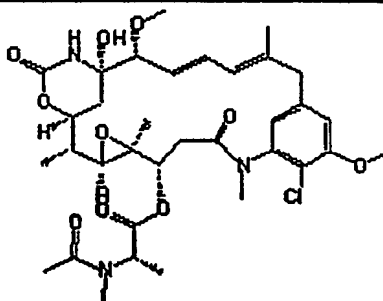
Maytansine/
Maytenus sp./
NSC-153858

35846-53-8/
other related
macrolides

cancer/
severe toxicity

tubulin
binding
agent (causes
extensive
disassembly
of the
microtubule
and totally
prevents
tubulin
spiralization)

Broad Activity in NCI
tumor panel (NSC-
153858; NSC-153858);
NCI tumor panel,
GI50's from 3 μ M to
0.1 pM; LC50's from
250 μ M to 10 pM. Two
different experiments
gave very different
potencies.



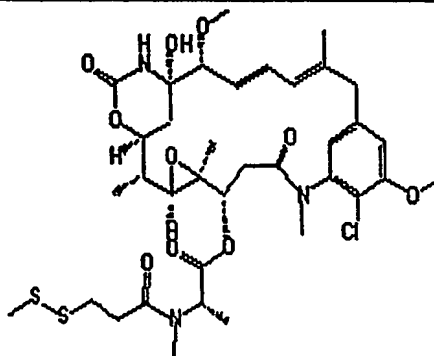
Maytansine-IgG(EGFR
directed)-conjugate¹¹/
semi-synthetic; starting
material from *Maytenus*
sp.

not reported/
other related
macrolides

breast, head and neck,
Squamous cell
carcinoma/
not reported

EGFR
binding and
tubulin
binding

not reported



Maytansine-IgG(CD56
antigen)-conjugate¹², 3.5
drug molecules per IgG/
semi-synthetic; starting
material from *Maytenus*

not reported/
other related
macrolides

Neuroendocrine, small-
cell lung, carcinoma/
mild toxicity (fatigue,
nausea, headaches and
mild peripheral

CD56
binding and
tubulin
binding

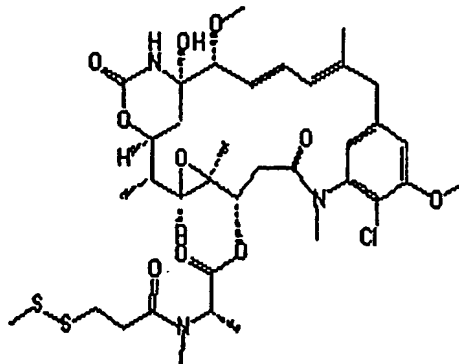
antigen-specific
cytotoxicity (cell
culture; epidermal,
breast, renal ovarian
colon) with IC50's of

FIG. 11M

sp./
huN901-DM1

neuropathy); no
hematological toxicity;
MTD 60 mg/Kg, I.V.,
weekly for 4 weeks; only
stable disease reported
(humans)

10-40 pM; animal
studies (mice SCLC
tumor--alone and in
combination with taxol
or cisplatin completely
eliminated tumors).



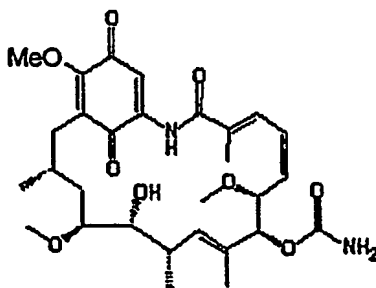
Maytansine-IgG(CEA
antigen)-conjugate¹³, 4
drug molecules per IgG/
semi-synthetic; starting
material from *Maytenus*
sp./
C424-DM1

not reported/
other related
macrolides

non-small-cell lung,
carcinoma pancreas,
lung, colon/
mild toxicity (fatigue,
nausea, headaches and
mild peripheral
neuropathy); pancreatic
lipase elevated; MTD 88
mg/Kg, I.V., every 21
days; only stable disease
reported (humans); t_{1/2}
was 44 hr.

CEA binding
and tubulin
binding

antigen-specific
cytotoxicity (cell
culture; epidermal,
breast, renal ovarian
colon) with IC₅₀'s of
10-40 pM; animal
studies (mice:
melanoma [COLO-
205]--alone and in
combination with taxol
or cisplatin completely
eliminated tumors);



Geldanamycin /
Streptomyces
hygroscopicus var.
Geldanus/
NSC-212518; Antibiotic
U 29135; NSC-122750

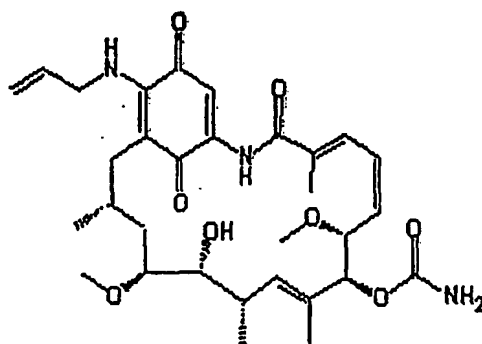
30562-34-6/
natural
derivatives

cancer/
not reported

binds Hsp 90
chaperone
and inhibits
function

NCI tumor panel (cell
culture); 5.3 to 100
nM; most active in
colon, lung and
leukemia. NCI tumor
panel, GI₅₀'s from 10
μM to 0.1 nM; LC₅₀'s
from 100 μM to 100
nM. Two assays with
very different potencies.

FIG. 11N



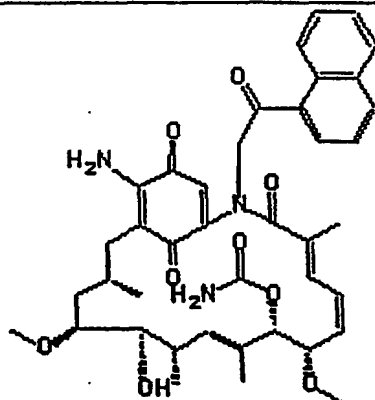
Geldanamycin Analog/
semi-synthetic; /
CP-127374; 17-AAG;
NSC-330507

745747-14-7/
Kosan, NCI
and UK
looking for
analogs with
longer t_{1/2}
and oral
activity;
analogs
include: NSC-
255110;
682300;
683661;
683663.

solid tumors/
Dose limiting toxicities
(anemia, anorexia,
diarrhea, nausea and
vomiting); t_{1/2} (i.v.) is
about 90 min; no
objective responses
measured at 88 mg/Kg
(i.v. daily for 5 days,
every 21 days);

binds Hsp 90
chaperone
and inhibits
function

cell culture (not
reported); animal
models active (tumor
regression observed) in
breast, ovary,
melanoma, colon.

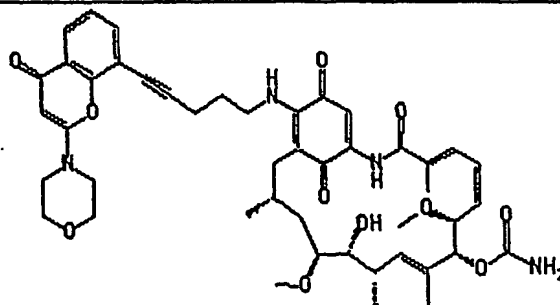


Geldanamycin analog/
semi-synthetic; /
CP-202567

not reported/
analogs
prepared

solid tumors/
not reported

binds Hsp 90
chaperone
and inhibits
function



Geldanamycin
conjugates/
semi-synthetic; /
LY-294002-GM; PI3K-1-
GM

345232-44-2/
analogs
prepared

breast/
not reported

binds Hsp 90
chaperone
and inhibits
function;
binds and

cell culture (no
reported); animal
models performed

FIG. 110

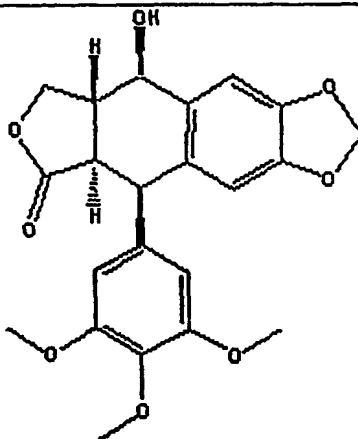
inhibits PI-3
kinase

Structure Not Reported

Geldanamycin Analog/ not reported/ CNF-101	not reported/ analogs prepared	breast, prostate/ not reported	binds Hsp 90 chaperone and inhibits function	not reported
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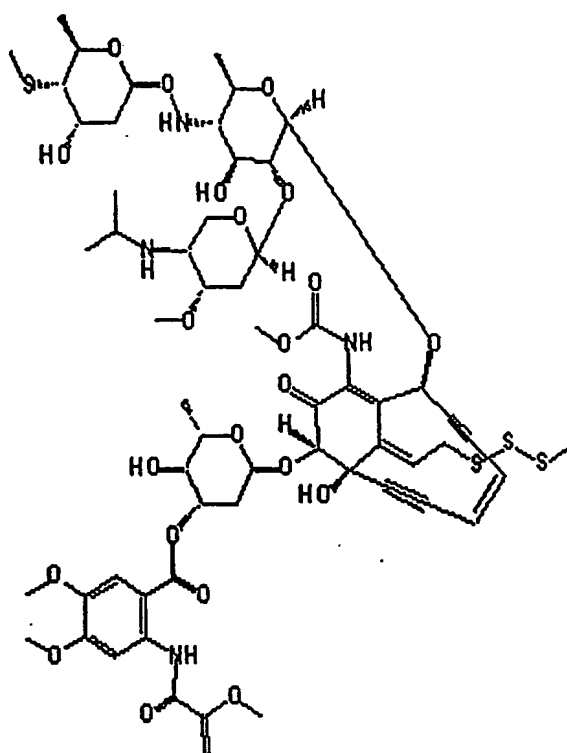
Structure Not Reported

Geldanamycin- testosterone conjugate/ semi-synthetic/ GMT-1	not reported/ analogs prepared	prostate/ not reported	binds Hsp 90 chaperone and inhibits function and testosterone receptors where it is internalized	not reported; conjugate has a 15-fold selective cytotoxicity for androgen positive prostate cells
--	--------------------------------------	---------------------------	---	---



Podophyllotoxin/ <i>Podophyllum</i> sp.	518-28-5/ many analogs	<i>Verruca vulgaris</i> , Condyloma/ severe toxicity when given i.v. or s.c.	tubulin inhibitor and topoisomer- ase inhibitor	broad activity (cell culture) with IC ₅₀ 's in μM range
--	---------------------------	---	--	--

FIG. 11P



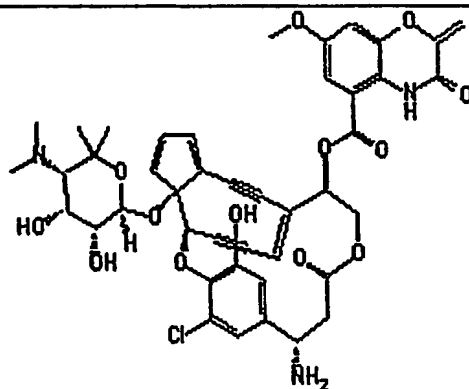
esperamicin-A1/
not known/
BBM-1675A1; BMY-
28175; GGM-1675

99674-26-7

cancer/
not reported (suspected
severe toxicity)

DNA
cleaving
agent

highly potent activity
(cell culture); animal
models highly potent
with optimal dose of
0.16 micrograms/Kg



C-1027¹⁴/
Streptomyces setonii C-
1027/
C-1027

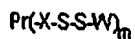
120177-69-7

cancer (examined
hepatoma, breast, lung
and leukemia/
not reported

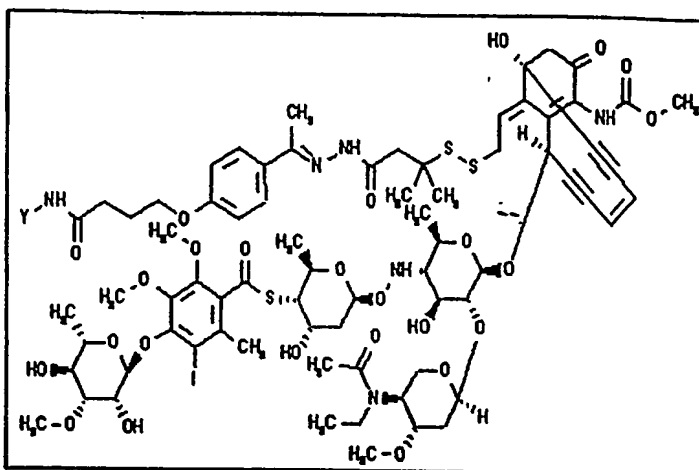
DNA
cleaving
agent

extremely potent (cell
culture) IC50's in pM
and fM; conjugated to
antibodies the potency
remains the same (ie.
5.5 to 42 pM);

FIG. 11Q



$m = 0.5 - 15$
 Pr = proteinaceous carrier
 W = calicheamicin minus Me-S-S-S
 X = linker
 Y = antibody P76.6



Calicheamicin-IgG(CD33 antigen)-conjugate^{15/}
 semi-synthetic:
Micromonospora echinospora
 gemtuzumab ozogamicin;
 mylotarg; WAY-CMA-676; CDP-771

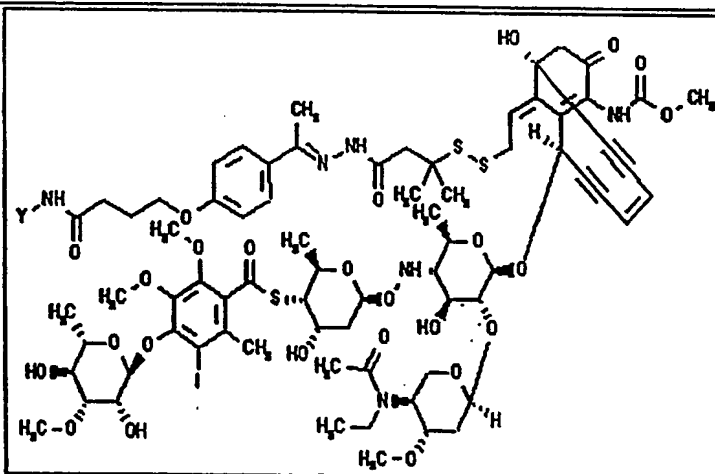
113440-58-7; AML/
 220578-59-6/ mild toxicity
 several
 reported in
 patents

DNA
 cleaving
 agent

Kills CD33+ cells (HL-60, NOMO-1, and NKM-1) at 100 ng/mL; MDR cell lines are not effected by the drug.



$m = 0.5 - 15$
 Pr = proteinaceous carrier
 W = calicheamicin minus Me-S-S-S
 X = linker
 Y = antibody P76.6



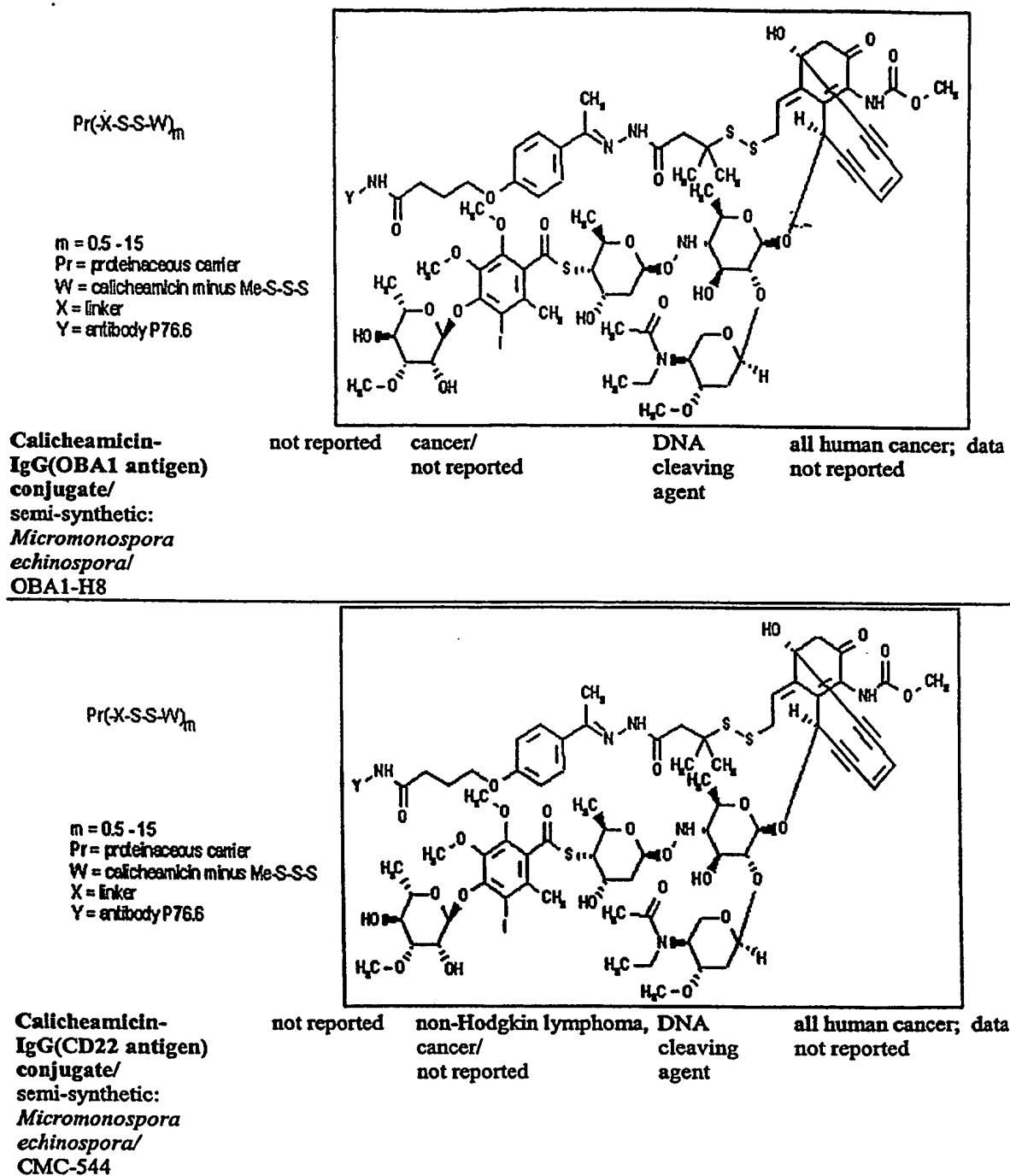
Calicheamicin-IgG-conjugates^{16/}
 semi-synthetic:
Micromonospora echinospora

113440-58-7; cancer/
 220578-59-6 not reported

DNA
 cleaving
 agent

TBD

FIG. 11R



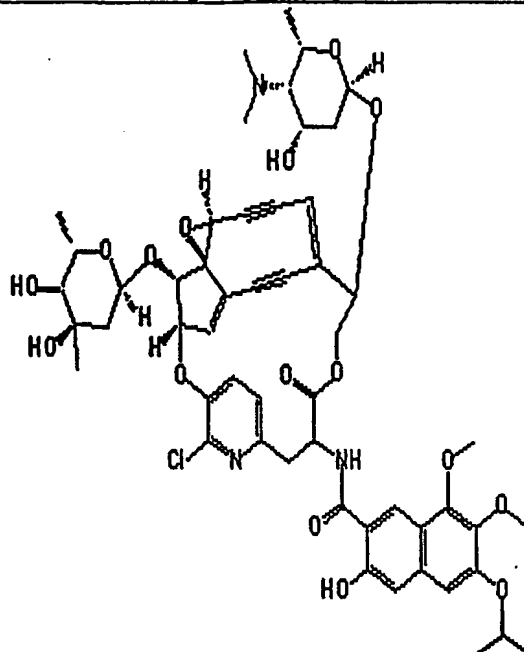
parially esterified polystyrene maleic acid copolymer (SMA)
 conjugated to neocarzinostatin (NCS)

Neocarzinostatin ¹⁷ / semi-synthetic; <i>Streptomyces</i> <i>carconistaticus</i> / Zinostatin stimalamer; YM-881; YM-16881	123760-07-6; liver cancer and brain 9014-02-2 cancer/ not reported	DNA cleaving agent	cell culture data not reported.
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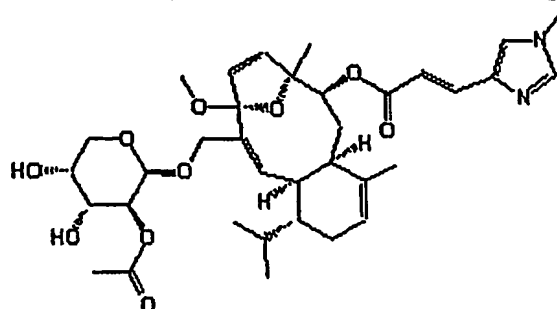
FIG. 11S

IgG (TES-23)-conjugated to neocarzinostatin

Neocarzinostatin/ not reported/ TES-23-NCS	not reported	solid tumors/ toxicity not reported; the TES-23 antibody (without anticancer agent) was as effective at eliminating tumors as the drug conjugated protein	DNA cleaving agent and immunostim- ulator	cell culture data not reported.
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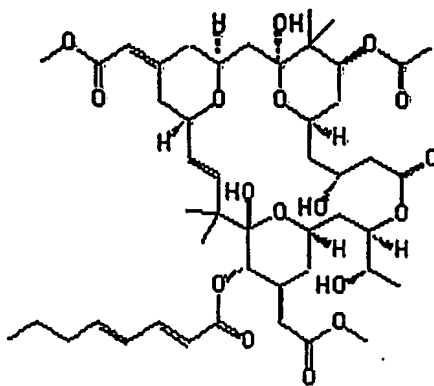


Kedarcidin ¹⁸ / <i>Streptoalloteichus</i> sp NOV strain L5856, ATCC 53650/ NSC-646276	128512-40-3; 128512-39-0/ chromophore and protein conjugate	cancer/ not reported	DNA cleaving agent	cell culture (IC ₅₀ 's in ng/mL); 0.4 HCT116; 0.3 HCT116/VP35; 0.3 HCT116/VM46; 0.2 A2780; 1.3 A2780/DDP. animal models in P388 and B-16 melanoma. NCI tumor panel, GI ₅₀ 's from 50 μM to 5 μM.
--	---	-------------------------	--------------------------	--



Eleutherobins/ marine coral	174545-76-7/ sarcodictyins (marine coral)	cancer/ not reported	tubulin binding agent	similar potency to taxol; not effective against MDR cell lines
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FIG. 11T

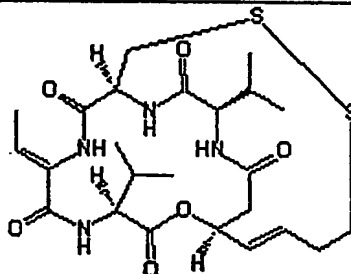


Bryostatin-1/
Bugula neritina (marine
bryozoan)/
GMY-45618; NSC-
339555

83314-01-6

leukemia, melanoma,
lung, cancer/
myalgia; accumulated
toxicity; poor water
solubility; dose limiting
toxicity

immunostim- not reported
ulant (TNF,
GMCSF,
etc);
enhances cell
kill by
current
anticancer
agents



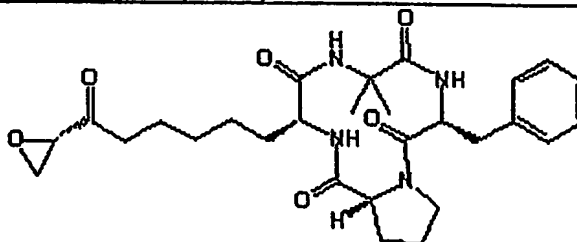
FR-901228/
Chromobacterium
violaceum strain 968/
NSC-63-176; FK-228

128517-07-7

leukemia, T-cell
lymphoma, cancer/
toxic doses (LD50) 6.4
and 10 mg/Kg, ip and iv
respectively; GI
toxicity, lymphoid
atrophy; dose limiting
toxicity (human) 18
mg/Kg; t1/2 of 8 hrs
(human)

histone
deacetylase
inhiibitor

In vitro cell lines (NCI
tumor panel);
IC50's of between 0.56
and 4.1 nM (breast,
lung, gastric colon,
leukemia)



Chlamydocin/
not reported

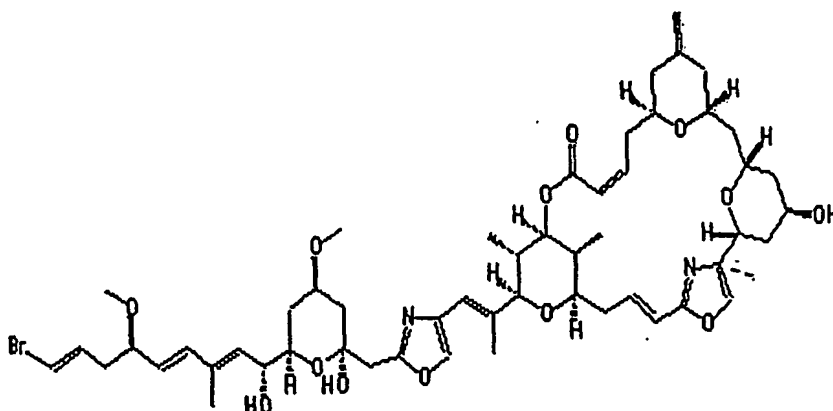
53342-16-8

cancer/
not reported

histone
deacetylase
inhiibitor

not reported (cell
culture);
inhibits histone
deacetylase at an IC50
of 1.3 nM

FIG. 11U

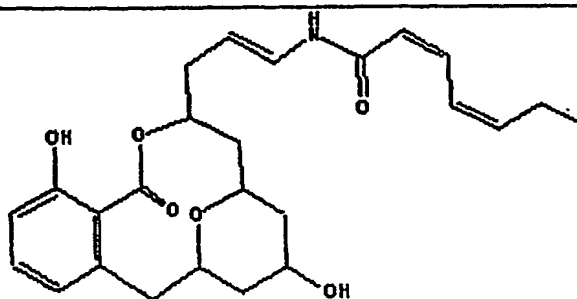


Phorboxazole A¹⁹
marine sponge

181377-57-1; leukemia, myeloma/
165689-31-6; not reported
180911-82-4;
165883-76-1/
analogs
prepared

not reported
(induces
apoptosis)

NCI tumor panel
(details not reported);
IC50's of 1-10 nM. The
inhibition values
(clonogenic growth of
human cancer cells) at
10 nM ranged from 6.2
to > 99.9% against
NALM-6 human B-
lineage acute
lymphoblastic
leukemia cells, BT-20
breast cancer cells and
U373 glioblastoma
cells, with the specified
compound showing
inhibition values in the
range of 42.4 to >
99.9% against these cell
lines.; IC50's are nM
for MDR cell lines.



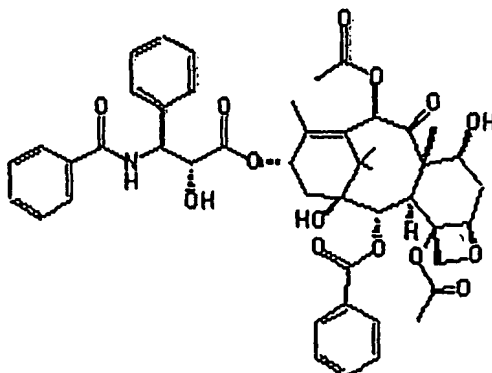
Apicularen A
Chondromyces robustus

220757-06-2/ cancer/
natural not reported
derivatives

not reported

IC50's of 0.1 to 3
ng/mL (KB-3-A, KB-
Va, K562, HL60, U937,
A498, A549, PV3 and
SK-OV3)

FIG. 11V

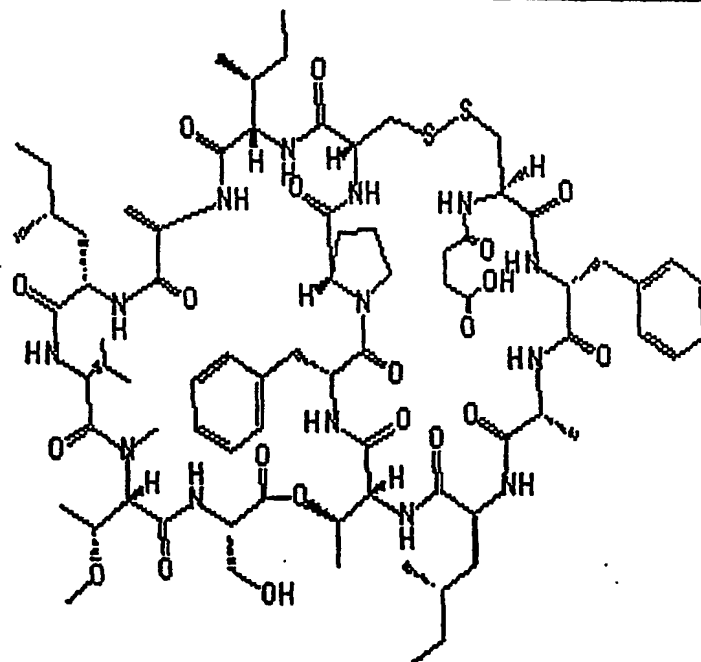


Taxol/
Pacific yew and fungi/
Paclitaxel; NSC-125973

33069624/
many analogs

cancer; breast, prostate, tubulin
ovary, colon, lung, head binding
& neck, etc./ agent
severe toxicity (grade III
and IV)

NCI tumor panel;
GI50's of 3 nM to 1
 μ M;
TGI 50 nM to 25 μ M



Vitilevuamide/
Didemnum cuculliferum
or *Polysyncrator*
lithostrotum

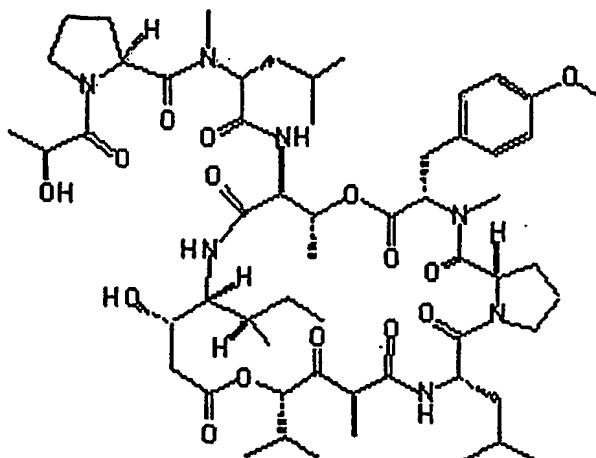
191681-63-7

cancer/
not reported

tubulin
binding
agent

cell culture; IC50's of
6-311 nM (panel of
tumor cell lines
HCT116 cells, A549
cells, SK-MEL-5 cells
A498 cells). The
increase in lifespan
(ILS) for CDF1 mice
after ip injection of
P388 tumor cells was in
the range of -45 to
+70% over the dose
range of 0.13 to 0.006
mg/kg.

FIG. 11W



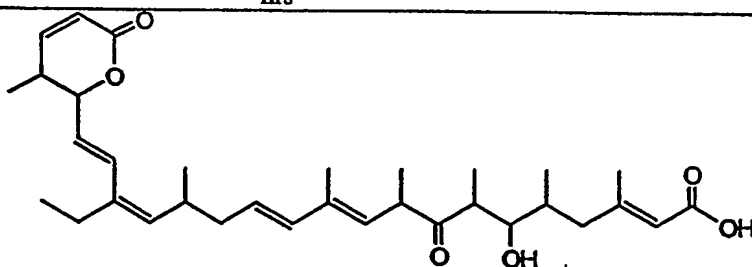
Didemnin B/
Trididemnum solidum/
NSC-2325319; IND
24505

77327-05-0;
77327-04-9;
77327-06-1/
other related
natural
products

non-Hodgkin's
lymphoma, breast,
carcinoma, CNS, colon/
Discontinued due to
cardiotoxicity; nausea,
neuro-muscular toxicity
and vomiting MTD 6.3
mg/Kg; toxicity
prevented achieving a
clinically signif. effect;
rapidly cleared (t_{1/2} 4.8
hrs

inhibits
protein
synthesis via
EF-1

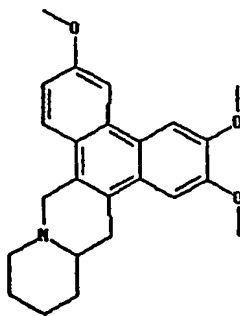
NCI 60-tumor panel
(GI50's): 100 nM to 50
fM.
Not potent against
MDR cell lines.



Leptomycin B/
Streptomyces sp. strain
ATS 1287/
NSC-364372; elactocin

87081-35-4

NCI 60-tumor panel
(GI50's):
8 μ M to 1 pM; (LC50):
250 μ M to 10 nM
(several cell lines at 0.1
nM). Two testing
results with very
different potencies.



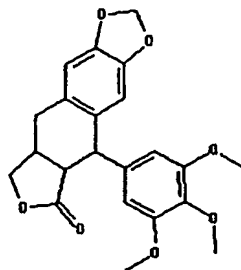
Cryptopleurin/

NCI 60-tumor panel

FIG. 11X

not known/
NSC-19912

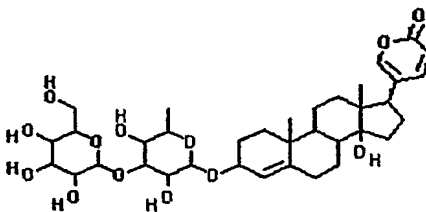
(GI50's): 19 nM to 1
pM; (LC50): 40 μ M to
10 nM (several cell
lines at 1 pM).



Silicicolin/
not known/
NSC-403148,
deoxypodophyllotoxin,
desoxypodophyllotoxin
podophyllotoxin,
deoxysilicicolin

19186-35-7

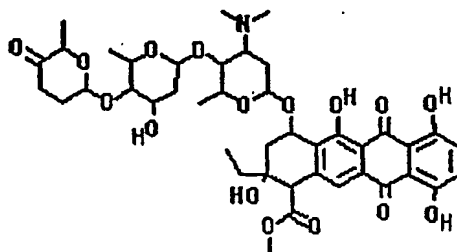
NCI 60-tumor panel
(GI50's): ~100 nM to 3
nM; (LC50): 50 μ M to
10 nM



Scillaren A/
not known/
NSC-7525; Gluco-
proscillaridin A;
Scillaren A

124-99-2

NCI 60-tumor panel
(GI50's): 50 nM to 0.1
nM;
(LC50): 250 μ M to 0.1
nM



Cinerubin A-HCl/
not known/
NSC-243022; Cinerubin
A hydrochloride;
CL 86-F2 HCl;
CL-86-F2-hydrochloride

not reported

NCI 60-tumor panel
(GI50's): 15 nM to 10
pM; (LC50): 100 μ M
to 6 nM

FIG. 11Y